Claims:

1. A method for designing a candidate polypeptide for expression in a suitable host, said method comprising,

identifying one or more hydrophobic peptide sequences within a polypeptide of interest, and

arranging or re-locating at least one of said hydrophobic peptide sequences within said polypeptide so as to generate said candidate polypeptide with reduced amplitude in hydrophobicity and/or length of any hydrophobic region(s).

2. The method of claim 1, wherein the polypeptide of interest is to be expressed in a bacterial host.

3. The method of claim 1 or 2, wherein the bacterial host is *E. coli*.

4. The method of claim 3, wherein the polypeptide is non-native to *E. coli*.

5. The method of any one of the preceding claims, wherein the polypeptide of interest comprises a non-natural polypeptide or a theoretical non-natural polypeptide.

6. The method of claim 5, wherein the polypeptide comprises a polyepitope polypeptide comprising a tandem array of epitopes of interest.

7. A method for designing a candidate polyepitope polypeptide comprising a tandem array of epitopes for expression in a suitable host, said method comprising,

identifying the relative hydrophobicity of each of said epitopes,

dividing said epitopes on the basis of said identified hydrophobicities into groups of substantially equivalent numbers, said groups comprising at least a first group of epitopes of most relative hydrophobicity and a second group of epitopes of least relative hydrophobicity, and

arranging epitopes from said first and second groups in a substantially alternating manner so as to generate said candidate polyepitope polypeptide with reduced amplitude in hydrophobicity and/or length of any hydrophobic region(s).

8. A method for designing a candidate polyepitope polypeptide comprising a tandem array of epitopes for expression in a suitable host, said method comprising,

identifying the relative hydrophobicity of each of said epitopes,

dividing said epitopes on the basis of said identified hydrophobicities into three groups of substantially equivalent numbers, said groups comprising a first group of epitopes of most hydrophobicity, a second group of epitopes of intermediate relative hydrophobicity, and a third group of epitopes of least relative hydrophobicity,

arranging epitopes from said first, second and third groups into triplets containing an epitope from each group, and

arranging said triplets in a linked sequence so as to generate said candidate polyepitope polypeptide with reduced amplitude in hydrophobicity and/or length of any hydrophobic region(s).

9. A method for designing a candidate polyepitope polypeptide comprising a tandem array of epitopes for expression in a suitable host, said method comprising,

identifying the relative hydrophobicity of each of said epitopes,

dividing said epitopes on the basis of said identified hydrophobicities into four groups of substantially equivalent numbers, said groups comprising a first group of epitopes of most hydrophobicity, a second group of epitopes of lesser relative hydrophobicity, a third group of epitopes of even lesser relative hydrophobicity, and a fourth group of least relative hydrophobicity

arranging epitopes from said first, second and third groups into quadruplets containing an epitope from each group, and

arranging said quadruplets in a linked sequence so as to generate said candidate polyepitope polypeptide with reduced amplitude in hydrophobicity and/or length of any hydrophobic region(s).

10. The method of any one of claims 7 to 9, wherein the polyepitope polypeptide comprises 5 to 100 epitopes.

11. The method of any one of claims 7 to 9, wherein the polyepitope polypeptide comprises 10 to 35 epitopes.

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AMENDED CLAIMS
[(received by the International Bureau on 12 November 2003 (12.11.03); original claim 13 amended; remaining claims unchanged (1 page)]

12. The method of any one of claims 7 to 11, wherein the epitopes comprising the polyepitope polypeptide are selected from epitopes of any one of the viruses of the group consisting of Epstein-Barr virus (EBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and cytomegalovirus (CMV).

13. A method of expressing a polypeptide in a suitable host, said method comprising,

designing a polypeptide in accordance with the method of any one of claims 1 to 12,

introducing a polynucleotide encoding said polypeptide into said host, such that said host is capable of expressing said polypeptide, and

culturing said host under conditions suitable for expression of said polypeptide.

14. A polypeptide designed in accordance with the method of any one of claims 1 to 5.

15. A polyepitope polypeptide designed in accordance with the method of any one of claims 1 to 12.

16. A polyepitope polypeptide comprising N epitopes, wherein N is any integer, said polyepitope polypeptide having the formula;

Triplet 1 - Triplet 2 - .... - Triplet N/3,

wherein each of said triplets comprises three linked epitopes selected by,

identifying and ranking the relative hydrophobicity of each of the N epitopes,

grouping the ranked N epitopes into three groups of substantially equivalent numbers, based upon the identified relative hydrophobicity of the N epitopes, to produce a first group comprising the epitopes of most relative hydrophobicity, a second group of epitopes of intermediate relative hydrophobicity, and a third group of epitopes of least relative hydrophobicity, and

selecting the epitopes for each of said triplets according to the following table:

	Epitope 1	Epitope 2	Epitope 3
Triplet 1 (N-terminal)	Most hydrophilic of Group 2	Most hydrophobic of Group 1	Most hydrophilic of Group 3
Triplet 2	2nd most hydrophilic of Group 2	2nd most hydrophobic of Group 1	2nd most hydrophilic of Group 3
Triplet N/3 (C-terminal)	Most hydrophobic of Group 2	Most hydrophilic of Group 1	Most hydrophobic of Group 3

17. The polyepitope polypeptide of claim 15 or 16, wherein the epitopes are contiguous or spaced apart by intervening sequences which are substantially free of sequences which naturally flank said epitopes.

18. A polypeptide vaccine comprising a polyepitope polypeptide according to any one of claims 14 to 17 and a pharmaceutically acceptable carrier and/or adjuvant.

19. A polyepitope polypeptide comprising an amino acid sequence substantially corresponding to an amino acid sequence selected from the group consisting of:

FLRGRAYGL – PYLFWLAAI – HRCQAIRKK – RRIYDLIEL – VQPPQLTLQV-GLCTLVAML - RLRAEAQVK -IEDPPFNSL –YLLEMLWRL – GQGGSPTAM - AVLLHEESM - IALYLQQNWWTL-RAKFKQLL - SSCSSCPLSKI- TYGPVFMCL-QAKWRLQTL - RPPIFIRRL- VSFIEFVGW - YPLHEQHGM –VEITPYKPTW - CLGGLLTMV – EENLLDFVRF - TYSAGIVQI – LLDFVRFMGV -EGGVGWRHW (SEQ ID NO:1),

FLRGRAYGL - PYLFWLAAI – HRCQAIRKK – RRIYDLIEL – GLCTLVAML – RLRAEAQVK - IEDPPFNSL –TYSAGIVQI - LLDFVRFMGV - EGGVGWRHW - IALYLQQNWWTL - RAKFKQLL – SSCSSCPLSKI - TYGPVFMCL - QAKWRLQTL-RPPIFIRRL - VSFIEFVGW – YPLHEQHGM – VEITPYKPTW – CLGGLLTMV – EENLLDFVRF - YLLEMLWRL – GQGGSPTAM - AVLLHEESM – VQPPQLTLQV (SEQ ID NO:2),

SSCSSCPLSKI – HRCQAIRKK – CLGGLLTMV – LTAGFLIFL – RLRAEAQVK – IEDPPFNSL – LLSAWILTA – RRRWRRLTV - PYLFWLAAI – YLLEMLWRL – GQGGSPTAM – VMSNTLLSAW – ALLVLYSFA – RAKFKQLL – IALYLQQNW – TYGPVFMCL - QAKWRLQTL – YLQQNWWTL – YPLHEQHGM – CPLSKILL (SEQ ID NO:3),

IPIVAIVALV – RLRPGGKKK – ILKEPVHGV – PLVKLWYQL – RPGGKKKYKL – KYKLKHIVW – TWETWWTEYW – EIKDTKEAL – KRWIILGLNK - KLWVTVYYGV – KIEELRQHL – MTNNPPIPV – VTLWQRPLV – WASRELERF – LLWKGEGAV – YTAFTIPSI – IYQEPFKNLK – SLYNTVATL – AIIRILQQL – AIFQSSMTK – VIYQYMDDL – LVGPTPVNI – TPQDLNTML – YLAWVPAHK – ALVEICTEM – TLNAWVKVV (SEQ ID NO:4),

and

LLFNILGGWV – KTSERSQPR – FLLLADARV – LLFLLLADA – RLGVRATRK – GVAGALVAFK – LPGCSFSIF – RMYVGGVEHR – VAGALVAFK – DLMGYIPLV – LIFCHSKKK – ILAGYGAGV – HMWNFISGI – QLFTFSPRR – VGIYLLPNR – FWAKHMWNF – YLVTRHADV – LSAFSLHSY – WMNRLIAFA – YLLPRRGPRL – YLVAYQATV – RLIVFPDLGV – TLGFGAYMSK – IPFYGKAI – VLVGGVLAA – CTCGSSDLY (SEQ ID NO:5).

20. The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

FLRGRAYGL – PYLFWLAAI – HRCQAIRKK – RRIYDLIEL – VQPPQLTLQV-GLCTLVAML - RLRAEAQVK -IEDPPFNSL –YLLEMLWRL – GQGGSPTAM - AVLLHEESM - IALYLQQNWWTL-RAKFKQLL - SSCSSCPLSKI- TYGPVFMCL-QAKWRLQTL - RPPIFIRRL- VSFIEFVGW - YPLHEQHGM –VEITPYKPTW - CLGGLLTMV – EENLLDFVRF - TYSAGIVQI – LLDFVRFMGV -EGGVGWRHW (SEQ ID NO:1).

21. The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

FLRGRAYGL - PYLFWLAAI – HRCQAIRKK – RRIYDLIEL – GLCTLVAML – RLRAEAQVK - IEDPPFNSL –TYSAGIVQI - LLDFVRFMGV - EGGVGWRHW - IALYLQQNWWTL - RAKFKQLL – SSCSSCPLSKI - TYGPVFMCL - QAKWRLQTL-RPPIFIRRL - VSFIEFVGW – YPLHEQHGM – VEITPYKPTW – CLGGLLTMV – EENLLDFVRF - YLLEMLWRL – GQGGSPTAM - AVLLHEESM – VQPPQLTLQV (SEQ ID NO:2).

22. The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

SSCSSCPLSKI – HRCQAIRKK – CLGGLLTMV – LTAGFLIFL – RLRAEAQVK – IEDPPFNSL – LLSAWILTA – RRRWRRLTV - PYLFWLAAI – YLLEMLWRL – GQGGSPTAM – VMSNTLLSAW – ALLVLYSFA – RAKFKQLL – IALYLQQNW – TYGPVFMCL - QAKWRLQTL – YLQQNWWTL – YPLHEQHGM – CPLSKILL (SEQ ID NO:3).

23. The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

IPIVAIVALV – RLRPGGKKK – ILKEPVHGV – PLVKLWYQL – RPGGKKKYKL – KYKLKHIVW – TWETWWTEYW – EIKDTKEAL – KRWIILGLNK - KLWVTVYYGV – KIEELRQHL – MTNNPPIPV – VTLWQRPLV – WASRELERF – LLWKGEGAV – YTAFTIPSI – IYQEPFKNLK – SLYNTVATL – AIIRILQQL – AIFQSSMTK – VIYQYMDDL – LVGPTPVNI – TPQDLNTML – YLAWVPAHK – ALVEICTEM – TLNAWVKVV (SEQ ID NO:4).

24. The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

LLFNILGGWV – KTSERSQPR – FLLLADARV – LLFLLLADA – RLGVRATRK – GVAGALVAFK – LPGCSFSIF – RMYVGGVEHR – VAGALVAFK – DLMGYIPLV – LIFCHSKKK – ILAGYGAGV – HMWNFISGI – QLFTFSPRR – VGIYLLPNR – FWAKHMWNF – YLVTRHADV – LSAFSLHSY – WMNRLIAFA – YLLPRRGPRL – YLVAYQATV – RLFVFPDLGV – TLGFGAYMSK – IPFYGKAI – VLVGGVLAA – CTCGSSDLY (SEQ ID NO:5).

25. A polypeptide vaccine comprising a polyepitope polypeptide according to any one of claims 19 to 24 and a pharmaceutically acceptable carrier and/or adjuvant.

26. A viral or DNA vaccine comprising a polynucleotide encoding a polypeptide designed in accordance with the method of any one of claims 1 to 12 and a pharmaceutically acceptable carrier and/or adjuvant.

27. A viral or DNA vaccine comprising a polynucleotide encoding a polypeptide according to any one of claims 19 to 24 and a pharmaceutically acceptable carrier and/or adjuvant.